

EXHIBIT B23

GYN-18-1020: Final Decision

Gynecologic Oncology <eesserver@eesmail.elsevier.com>

Wed 9/19/2018 1:26 PM

Deleted Items

To:Ghassan Saed <gsaed@med.wayne.edu>;

Cc:Nicole King <nfletche@med.wayne.edu>; Ira Memaj <ira.memaj@wayne.edu>; Robert Morris <rmorris@med.wayne.edu>; akharp627@gmail.com <akharp627@gmail.com>; Amy Harper <aharper4@med.wayne.edu>; florrie1522@gmail.com <florrie1522@gmail.com>;

Ms. No.: GYN-18-1020

Title: Molecular basis supporting the association of talcum powder use with increased risk of ovarian cancer

Corresponding Author: Dr. Ghassan M. Saed

Authors: Nicole M Fletcher, Ph.D.; Ira Memaj, M.S.; Rong Fan, M.S.; Amy K Harper, M.D.; Robert T Morris, M.D.;

Dear Dr. Saed,

Your paper, referenced above, has now been reviewed by at least two experts in the field and the Editors. Based on the reviewers' comments, we must inform you that while your work is not without merit, we are unable to accept your manuscript for publication in Gynecologic Oncology. In the last year we have seen a significant increase in the number of manuscripts submitted to the Journal and as a result, we are now accepting less than 20% of the manuscripts submitted to the Gynecologic Oncology.

We have attached the comments of the reviewers below in order for you to understand the basis for our decision. We hope that their thoughtful comments will help you in your future studies and possibly, with submission to another journal. Please note that a revised version of the current manuscript should not be submitted for another review to Gynecologic Oncology .

The critique of this paper in no way implies a lack of interest in this area of research, and we invite you to submit your future work to the Journal.

Sincerely,

Robert E. Bristow, MD
Editor
Gynecologic Oncology

Editorial Office
Elsevier



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Reviewers' comments:

Reviewer #1: The stated objective of the study by Fletcher and colleagues is to determine the effects of talc on expression of key inflammatory and redox markers in ovarian cancer and normal cell lines. Normal ovarian and EOC cells were treated with various doses of talc for 48 hours. Levels of CA-125 and selected key redox enzymes were measured using real-time RT-PCR and ELISA.

Overall this is a well-written manuscript and the conclusions are supported by the results. This is an important but controversial topic in need of rigorous scientific inquiry. The current *in vitro* study does provide novel information, but there are also some important limitations described below:

1. The significance of this study would be greatly enhanced if a mouse model corroborated the cell line findings. In this reviewer's opinion the cell line studies alone and the increase in CA-125 while intriguing are not sufficiently convincing.
2. The significance of SNP alterations should be further clarified
3. The first bulleted highlight, "Oxidative stress is a key mechanism to the initiation and progression of ovarian cancer" is not supported by this investigation and should be omitted.

Reviewer #2: The objective of this study was to investigate the effects of talc on inflammation and redox markers in ovarian cancer and normal cell lines. Talc-treated carcinoma cell lines and normal ovarian cells had a significant dose-dependent increase in the levels of the pro-oxidants inducible nitric oxide synthase (iNOS), nitrate/nitrite and myeloperoxidase (MPO), as well as CA 125, and decrease in the levels of the antioxidants CAT, SOD3, GSR, and GPX. Induction of mutations in key-enzymes affecting their activity was found in talc-treated cells compared to controls.

While the authors compellingly show changes in several key-enzymes regulating redox potential in cells exposed to talc, their data do not show, despite the authors' claim, any evidence that these cells are transformed. Specifically, no experiments documenting changes in cell survival, proliferation or resistance to apoptosis have been performed. Consequently, neither tumor initiation nor progression is documented in this study, as opposed to the statement in Highlight # 1 and elsewhere. While changes in redox potential play an important role in tumor biology in general, the present data are insufficient to back up the claim that talcum is central to the development of ovarian cancer.

Other comments:

The introduction should be better organized, with shorter description of the general features of ovarian cancer, replaced by a brief overview of redox proteins in cancer, followed by a discussion of their role in ovarian cancer.

The fact that SNPs were changed following such short exposure to talcum is surprising and makes one wonder what the biological effect of such changes might be.

References are in inconsistent style, some missing data (e.g. volume and page in # 7)